Emerging Resistance to Quinolones among Salmonella Typhi isolates in the United States, 1999-2001

Reller M, McClellan J, Joyce K, Polyak C, Mintz E, Angulo F, and the NARMS Woring Group

Background: Each year an estimated 800 persons in the United States are infected with *Salmonella* Typhi. Effective antimicrobial treatment, now commonly with ciprofloxacin (a fluoroquinolone), has reduced mortality from 20% to less than 1%. Resistance to nalidixic acid (a quinolone) is correlated with decreased susceptibility to ciprofloxacin (MIC > 0.12µg/ml); recent evidence suggests that patients infected with *Salmonella* Typhi with decreased susceptibility to ciprofloxacin respond poorly to therapy.

Methods: Since 1999, state and local public health laboratories participating in the National Antimicrobial Resistance Monitoring System submit *Salmonella* Typhi isolates received from clinical laboratories to the Centers for Disease Control and Prevention (CDC). At CDC, susceptibility testing to nalidixic acid and ciprofloxacin is performed by broth microdilution (Sensititre®).

Results: From 1999-2001, 554 S. Typhi isolates were tested and 135 (24%) were resistant to nalidixic acid; 2001 data are preliminary. Although no isolates were resistant to ciprofloxacin (MIC = $4\mu g/ml$), 130 (96%) of nalidixic acid-resistant isolates had decreased susceptibility to ciprofloxacin. Nalidixic acid resistance increased from 19% (31/166) in 1999 to 30% (63/211) in 2001. Of 124 patients from whom nalidixic acid-resistant *Salmonella* Typhi was isolated and clinical information complete, 96 (77%) isolates were from blood, 51 (41%) patients were female and the median age of patients was 22.5 years (range 1-75).

Conclusions: Clinicians should be aware that a high proportion of Salmonella Typhi isolates in the United States are resistant to nalidixic acid, which may portend clinical fluoroquinolone failure. Continued laboratory surveillance is essential to track emerging resistance. Correlation of in-vitro susceptibility and clinical outcomes will be required to inform decisions about breakpoints for ciprofloxacin and guidelines regarding appropriate empirical treatment for typhoid fever.

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